

**Amendments to the Claims:**

1. (Currently amended) An antibacterial compound consisting of a substantially uncharged morpholino antisense oligomer containing from 8 10 to 40 nucleotide subunits, each of said subunits comprising a morpholino ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base, said base-pairing moieties including a targeting nucleic acid sequence at least 10 nucleotides in length which is able to stably hybridize complementary to a bacterial 16S or 23S rRNA nucleic acid sequence, wherein

~~each of said subunits comprises a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base in the bacterial nucleic acid sequence, and~~

adjacent subunits are linked together by phosphorous-containing linkages, one to three atoms long, joining the morpholino nitrogen of one subunit to the 5' exocyclic carbon of an adjacent subunit, and ~~joined by uncharged linkages selected from the group consisting of: uncharged phosphoramidate and phosphorodiamidate, carbonate, carbamate, amide, phosphotriester, alkyl phosphonate, siloxane, sulfone, sulfonamide, sulfamate, thioformacetyl, and methylene-N-methylhydroxylamino, or by charged linkages selected from the group consisting of phosphate, charged phosphoramidate and phosphorothioate, wherein the ratio of uncharged linkages to charged linkages in the oligomer is at least~~ [[4]]5:1.

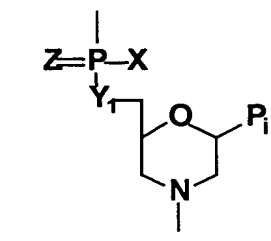
2. (Original) The compound of claim 1, wherein said oligomer is able to hybridize with the bacterial sequence at a  $T_m$  substantially greater than the  $T_m$  of a duplex composed of a corresponding DNA and the same bacterial sequence.

3. (Original) The compound of claim 1, wherein said oligomer is able to hybridize with the bacterial sequence at a  $T_m$  substantially greater than 37°C.

4. (Currently amended) The compound of claim 1, wherein said bacterial nucleic acid sequence is a 16S or 23S rRNA nucleic acid sequence of one of more bacteria selected from the group consisting of *Escherichia coli*, *Salmonella thyphimurium*, *Pseudomonas*

*aeruginosa*, *Vibrio cholera*, *Neisseria gonorrhoea*, *Staphylococcus aureus*, *Mycobacterium tuberculosis*, *Helicobacter pylori*, *Streptococcus pneumoniae*, *Treponema palladium*, *Chlamydia trachomatis*, *Bartonella henselae*, *Hemophilis influenza*, *Shigella dysenteriae*, *Enterococcus faecium*, and *Listeria monocytogenes* oligomer is a morpholine oligomer.

5. (Currently amended) The compound of claim 1, wherein each the uncharged linkages are selected from the group consisting of the structures presented in Figures 2A through 2D is an uncharged phosphorodiamidate linkage, in accordance with the structure below, where  $X=NR_2$ , R is hydrogen or methyl,  $Y_1=O$ ,  $Z=O$ , and  $P_i$  is a purine or pyrimidine base pairing moiety effective to bind, by base specific hydrogen bonding, to a base in a polynucleotide.



6. (Currently amended) The compound of claim 5, wherein each uncharged linkage, if present, is a linkage in accordance with the structure of claim 4, wherein X is oxide ( $-O^-$ ) or sulfide ( $-S^-$ ) phosphorodiamidate linkage as represented at Figure 2B, where  $X=NR_2$ , where R is hydrogen or methyl,  $Y=O$ , and  $Z=O$ .

7. (Currently amended) The compound of claim [[4]] 5, wherein each linkage is a phosphorodiamidate linkage as represented therein at Figure 2B, where  $X=NR_2$ , where R is hydrogen or methyl,  $Y=O$ , and  $Z=O$ .

8. (Currently amended) The compound of claim 1, wherein the region of complementarity with the target RNA sequence has a length of 13 to 20 bases the ratio of uncharged linkages to charged linkages in the oligomer is at least 8:1.

9. (Original) The compound of claim 1, wherein the antisense oligomer has a length of from 12 to 25 subunits.

10. (Currently amended) The compound of claim 7 ~~9~~, having a length of 15 to 20 subunits.

11. (Original) The compound of claim 1, wherein the targeting sequence is selected from the group consisting of SEQ ID NOs: 15, 16, and 21-25.

12. (Original) The compound of claim 1, where the targeting sequence is complementary to a Gram-positive bacterial 16S rRNA consensus sequence or a Gram-negative bacterial 16S rRNA consensus sequence.

13. (Original) The compound of claim 12, where the targeting sequence is selected from the group consisting of SEQ ID NOs: 27-30.

14. (Original) The compound of claim 1, wherein the targeting sequence is SEQ ID NO: 92.

15. (Currently amended) A method of treating a bacterial infection in a human or mammalian animal subject, comprising  
administering to the subject, in a pharmaceutically effective amount, a substantially uncharged morpholino antisense oligomer containing from ~~8~~ 10 to 40 nucleotide subunits, each of said subunits comprising a morpholino ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base, said base-pairing moieties including a targeting nucleic acid sequence at least 10 nucleotides in length which is able to stably hybridize ~~complementary~~ to a bacterial 16S or 23S rRNA nucleic acid sequence, wherein

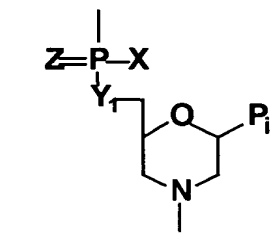
~~each of said subunits comprises a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base in the bacterial nucleic acid sequence, and~~

adjacent subunits are linked together by phosphorous-containing linkages, one to three atoms long, joining the morpholino nitrogen of one subunit to the 5' exocyclic carbon of an adjacent subunit, and joined by uncharged linkages selected from the group consisting of: uncharged phosphoramidate and phosphorodiamidate, carbonate, carbamate, amide, phosphotriester, alkyl phosphonate, siloxane, sulfone, sulfonamide, sulfamate, thioformacetyl, and methylene-N-methylhydroxylamino, or by charged linkages selected from the group consisting of phosphate, charged phosphoramidate and phosphorothioate, wherein the ratio of uncharged linkages to charged linkages in the oligomer is at least [[4]]5:1.

16. (Original) The method of claim 15, wherein said oligomer is able to hybridize with the bacterial sequence at a  $T_m$  substantially greater than 37°C.

17. (Currently amended) The method of claim 15, wherein the bacterial nucleic acid sequence is a 16S or 23S rRNA nucleic acid sequence of one of more bacteria selected from the group consisting of *Escherichia coli*, *Salmonella thyphimurium*, *Pseudomonas aeruginosa*, *Vibrio cholera*, *Neisseria gonorrhoea*, *Staphylococcus aureus*, *Mycobacterium tuberculosis*, *Helicobacter pylori*, *Streptococcus pneumoniae*, *Treponema palladium*, *Chlamydia trachomatis*, *Bartonella henselae*, *Hemophilis influenza*, *Shigella dysenteriae*, *Enterococcus faecium*, and *Listeria monocytogenes* oligomer is a morpholino-oligomer.

18. (Currently amended) The method of claim 16, wherein each the uncharged linkages are selected from the group consisting of the structures presented in Figures 2A through 2D is an uncharged phosphorodiamidate linkage, in accordance with the structure below, where  $X=NR_2$ , R is hydrogen or methyl,  $Y_1=O$ ,  $Z=O$ , and  $P_i$  is a purine or pyrimidine base pairing moiety effective to bind, by base specific hydrogen bonding, to a base in a polynucleotide.



19. (Currently amended) The method of claim 18, wherein each ~~uncharged linkage, if~~ present, is a linkage in accordance with the structure of claim 4, wherein X is oxide ( $-O^-$ ) or sulfide ( $-S^-$ ) phosphorodiamidate linkage as represented at Figure 2B, where  $X=NR_2$ , where R is hydrogen or methyl,  $Y=O$ , and  $Z=O$ .

20. (Currently amended) The method of claim ~~17~~ 18, wherein each linkage is a phosphorodiamidate linkage as represented therein at Figure 2B, where  $X=NR_2$ , where R is hydrogen or methyl,  $Y=O$ , and  $Z=O$ .

21. (Original) The method of claim 15, where the antisense oligomer has a length of from 12 to 25 bases.

22. (Currently amended) The method of claim 17, wherein the the region of complementarity with the target RNA sequence has a length of 13 to 20 bases ~~oligomer has a length of from 15 to 20 bases.~~

23. (Original) The method of claim 15, wherein the targeting sequence is selected from the group consisting of SEQ ID NOs: 15, 16 and 21-25.

24. (Original) The method of claim 15, where the targeting sequence is complementary to a Gram-positive bacterial 16S rRNA consensus sequence or a Gram-negative bacterial 16S rRNA consensus sequence.

25. (Original) The method of claim 24, where the targeting sequence is selected from the group consisting of SEQ ID NOs: 27-30.

26. (Original) The method of claim 21, for use in treatment of an infection produced by *E. coli*, *Salmonella thyphimurium*, *Pseudomonas aeruginosa*, *Vibrio cholera*, *Neisseria gonorrhoea*, *Helicobacter pylori*, *Bartonella henselae*, *Hemophilis Influenza*, *Shigella dysenterae*, *Staphylococcus aureus*, *Mycobacterium tuberculosis*, *Streptococcus pneumoniae*, *Treponema palladium* and *Chlamydia trachomatis*, where the antisense oligomer has a sequence selected from the group consisting of SEQ ID NOs: 21-25.

27. (Original) The method of claim 15, wherein the antisense oligomer is administered in an amount and manner effective to result in a peak blood concentration of at least 200-400 nM antisense oligomer.

28. (Original) The method of claim 15, for treating bacterial infections of the skin, wherein said administering is by a topical route.

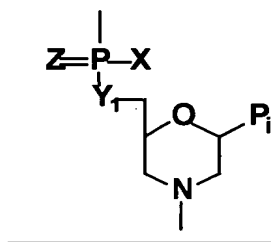
29. (Original) The method of claim 12, for use in treating a bacterial respiratory infection, wherein said administering is by inhalation.

30. (Currently amended) A livestock and poultry food composition containing a food grain supplemented with a subtherapeutic amount of an antibacterial compound, said compound consisting of a substantially uncharged morpholino antisense oligomer containing from 8 10 to 40 nucleotide subunits, each of said subunits comprising a morpholino ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base, said base-pairing moieties including a targeting nucleic acid sequence at least 10 nucleotides in length which is able to stably hybridize complementary to a bacterial 16S or 23S rRNA nucleic acid sequence, wherein ~~each of said subunits comprises a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base in the bacterial nucleic acid sequence, and~~ adjacent subunits are linked together by phosphorous-containing linkages, one to three atoms long, joining the morpholino nitrogen of one subunit to the 5' exocyclic carbon of an adjacent subunit, and joined by uncharged linkages selected from the group consisting of: uncharged phosphoramidate and phosphorodiamidate, carbonate, carbamate,

~~amide, phosphotriester, alkyl phosphonate, siloxane, sulfone, sulfonamide, sulfamate, thioformacetyl, and methylene N-methylhydroxylamino, or by charged linkages selected from the group consisting of phosphate, charged phosphoramidate and phosphorothioate, wherein the ratio of uncharged linkages to charged linkages in the oligomer is at least~~ [[4]]5:1.

31. (Currently amended) The composition of claim 30, wherein the bacterial nucleic acid sequence is a 16S or 23S rRNA nucleic acid sequence of one of more bacteria selected from the group consisting of *Escherichia coli*, *Salmonella thyphimurium*, *Pseudomonas aeruginosa*, *Vibrio cholera*, *Neisseria gonorrhoea*, *Staphylococcus aureus*, *Mycobacterium tuberculosis*, *Helicobacter pylori*, *Streptococcus pneumoniae*, *Treponema palladium*, *Chlamydia trachomatis*, *Bartonella henselae*, *Hemophilis influenza*, *Shigella dysenteriae*, *Enterococcus faecium*, and *Listeria monocytogenes* oligomer is a morpholino oligomer.

32. (Currently amended) The composition of claim 31, wherein each linkage is a phosphorodiamidate linkage ~~as represented at Figure 2B, in accordance with the structure below~~, where  $X=NR_2$ , where R is hydrogen or methyl,  $Y=O$ , and  $Z=O$ , and  $P_i$  is a purine or pyrimidine base pairing moiety effective to bind, by base specific hydrogen bonding, to a base in a polynucleotide.



33. (Original) The composition of claim 30, wherein the antisense oligomer has a length of from 12 to 25 bases.

34. (Original) The composition of claim 30, wherein the targeting sequence is selected from the group consisting of SEQ ID NOs: 15, 16, 21-25 and 27-30.